

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of)	
)	
Eva Turley)	Group Art Unit: unknown
)	
Serial No. Unknown)	
(Divisional of 09/210,896))	Examiner: unknown
)	
Filed: concurrently herewith)	
)	
For: Enhanced Affinity Hyaluronan)	
Binding Peptides)	

The Commissioner of Patents
& Trademarks
Washington, D.C. 20231
U.S.A.

Dear Sir:

PRELIMINARY AMENDMENT

We are simultaneously filing herewith a divisional application of United States serial no. 09/210,896 filed on December 16, 1998. Please enter the following amendment in the divisional application.

In the Specification:

Please amend page 1, lines 3 to 5 as follows:

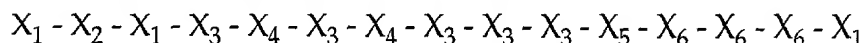
This application is a divisional of U.S. Patent Application Serial no. 09/210,896 filed on December 16, 1998 which claims the benefit under 35 USC§119(e) of United States provisional application serial no. 60/068,285, filed on December 19, 1997.

In the Claims:

Please delete claims 1-12 currently of record leaving claims 13-28 pending in the divisional application. Please amend claims 13, 16-25, 27 and 28 as follows. Please calculate the claim fee after the present amendment is entered.

13. (Amended) An isolated nucleic acid molecule encoding a HA binding peptide comprising:

(a) a sequence of the formula I:



wherein

each X_1 is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

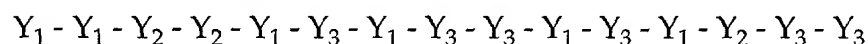
each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:



wherein

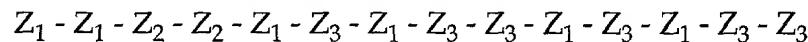
each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:



wherein

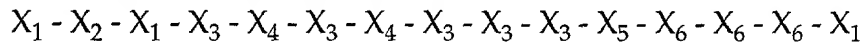
each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z_3 is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

16. (Amended) A method of modulating cell locomotion comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides to a cell or animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:



wherein

each X_1 is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

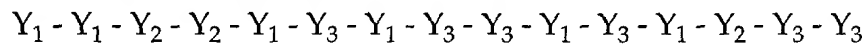
each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:



wherein

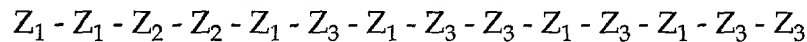
each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:



wherein

each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z_3 is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

17. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding peptide (HA

binding) to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence TMTRPHFHKRQLVLS.

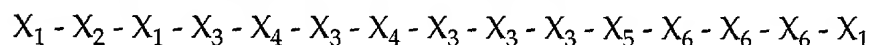
18. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSCHH.

19. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHH.

20. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHHV.

21. (Amended) A method of preventing or inhibiting tissue fibrosis comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides to an animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:



wherein

each X_1 is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:

$Y_1 - Y_1 - Y_2 - Y_2 - Y_1 - Y_3 - Y_1 - Y_3 - Y_3 - Y_1 - Y_3 - Y_1 - Y_2 - Y_3 - Y_3$

wherein

each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:

$Z_1 - Z_1 - Z_2 - Z_2 - Z_1 - Z_3 - Z_1 - Z_3 - Z_3 - Z_1 - Z_3 - Z_1 - Z_3 - Z_3$

wherein

each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z_3 is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

22. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence TMTRPHFHKRQLVLS.

23. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSCHH.

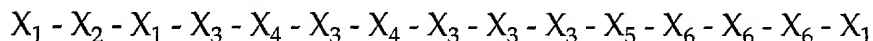
24. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHH.

25. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA

binding) peptide to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHHV.

27. (Amended) A method of treating or preventing cancer comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides to an animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:



wherein

each X_1 is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

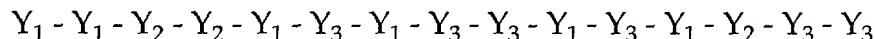
each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:



wherein

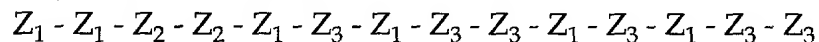
each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:



wherein

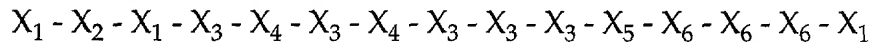
each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z_3 is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

28. (Amended) A method of preventing or reducing the metastasis of cancer cells comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides to an animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:



wherein

each X_1 is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

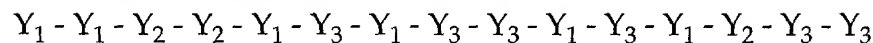
each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:



wherein

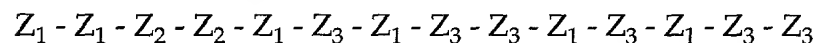
each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:



wherein

each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z_3 is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

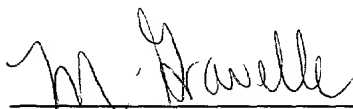
REMARKS

By the present amendment, claims 13-28 have been amended to remove the claim dependencies on the deleted claims and to incorporate the subject matter of the deleted claims where appropriate. The amendment does not contain new matter. Please enter the amendment prior to calculating the claim fees.

Entry of the above preliminary amendment is respectfully requested.

Respectfully submitted,

EVA TURLEY

A handwritten signature in cursive script, appearing to read "M. Gravelle", is written over a horizontal line.

Micheline Gravelle
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Dated: June 18, 2001

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph at page 1, lines 3 to 5 has been amended as follows:

This application is a divisional of U.S. Patent Application Serial no. 09/210,896 filed on December 16, 1998 which [This] claims the benefit under 35 USC§119(e) of United States provisional application serial no. 60/068,285, filed on December 19, 1997.

In the Claims:

Claims 1-12 have been cancelled.

Claims 13-28 are now pending in the divisional application.

Claims 13, 16-25, 27 and 28 have been amended as follows

13. (Amended) An isolated nucleic acid molecule encoding a HA binding peptide [according to claim 1] comprising:

(a) a sequence of the formula I:

X₁-X₂-X₁-X₃-X₄-X₃-X₄-X₃-X₃-X₃-X₅-X₆-X₆-X₆-X₁

wherein

each X₁ is independently selected from a hydroxy amino acid residue;

each X₂ is independently selected from a sulfur containing amino acid residue;

each X₃ is independently selected from a basic amino acid residue;

each X₄ is independently selected from an imino or aromatic amino acid residue;

each X₅ is independently selected from a dicarboxylic acid amino acid residue; and

each X₆ is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:

Y₁-Y₁-Y₂-Y₂-Y₁-Y₃-Y₁-Y₃-Y₃-Y₁-Y₃-Y₁-Y₂-Y₃-Y₃

wherein

each Y₁ is independently selected from a hydroxy amino acid residue;

each Y₂ is independently selected from a sulfur containing amino acid residue; and

each Y₃ is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:

Z₁-Z₁-Z₂-Z₂-Z₁-Z₃-Z₁-Z₃-Z₃-Z₁-Z₃-Z₁-Z₃-Z₃

wherein

each Z₁ is independently selected from a hydroxy amino acid residue;

each Z₂ is independently selected from a sulfur containing amino acid residue; and

each Z₃ is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

16. (Amended) A method of modulating cell locomotion comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides [according to claim 1] to a cell or animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:

X₁-X₂-X₁-X₃-X₄-X₃-X₄-X₃-X₃-X₃-X₅-X₆-X₆-X₆-X₁

wherein

each X₁ is independently selected from a hydroxy amino acid residue;

each X₂ is independently selected from a sulfur containing amino acid residue;

each X₃ is independently selected from a basic amino acid residue;

each X₄ is independently selected from an imino or aromatic amino acid residue;

each X₅ is independently selected from a dicarboxylic acid amino acid residue; and

each X₆ is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:

Y₁-Y₁-Y₂-Y₂-Y₁-Y₃-Y₁-Y₃-Y₃-Y₁-Y₃-Y₁-Y₂-Y₃-Y₃

wherein

each Y₁ is independently selected from a hydroxy amino acid residue;

each Y₂ is independently selected from a sulfur containing amino acid residue; and

each Y₃ is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:

Z₁-Z₁-Z₂-Z₂-Z₁-Z₃-Z₁-Z₃-Z₃-Z₁-Z₃-Z₁-Z₃-Z₃

wherein

each Z₁ is independently selected from a hydroxy amino acid residue;

each Z₂ is independently selected from a sulfur containing amino acid residue; and

each Z₃ is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

17. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding peptide (HA binding) [according to claim 3] to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence TMTRPHFKRQLVLS.

18. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide [according to claim 6] to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSCHH.

19. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide [according to claim 9] to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHH.

20. (Amended) A method of modulating cell locomotion according to claim 16 comprising administering an effective amount of hyaluronan-binding (HA binding)

peptide [according to claim 11] to a cell or animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHHV.

21. (Amended) A method of preventing or inhibiting tissue fibrosis comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides [according to claim 1] to an animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:

$X_1 - X_2 - X_1 - X_3 - X_4 - X_3 - X_4 - X_3 - X_3 - X_3 - X_5 - X_6 - X_6 - X_1$

wherein

each X_1 is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:

$Y_1 - Y_1 - Y_2 - Y_2 - Y_1 - Y_3 - Y_1 - Y_3 - Y_3 - Y_1 - Y_3 - Y_1 - Y_2 - Y_3 - Y_3$

wherein

each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:

$Z_1 - Z_1 - Z_2 - Z_2 - Z_1 - Z_3 - Z_1 - Z_3 - Z_3 - Z_1 - Z_3 - Z_1 - Z_3 - Z_3$

wherein

each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z₃ is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

22. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide [according to claim 3] to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence TMTRPHFHKRQLVLS.

23. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide [according to claim 6] to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSCHH.

24. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide [according to claim 9] to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHH.

25. (Amended) A method of preventing or inhibiting tissue fibrosis according to claim 21 comprising administering an effective amount of hyaluronan-binding (HA binding) peptide [according to claim 11] to an animal in need thereof, wherein said HA binding peptide comprises the amino acid sequence STMMSRSHKTRSHHV.

27. (Amended) A method of treating or preventing cancer comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides [according to claim 1] to an animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:

X₁ - X₂ - X₁ - X₃ - X₄ - X₃ - X₄ - X₃ - X₃ - X₃ - X₅ - X₆ - X₆ - X₆ - X₁

wherein

each X₁ is independently selected from a hydroxy amino acid residue;

each X₂ is independently selected from a sulfur containing amino acid residue;

each X₃ is independently selected from a basic amino acid residue;

each X₄ is independently selected from an imino or aromatic amino acid residue;

each X₅ is independently selected from a dicarboxylic acid amino acid residue; and

each X₆ is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:

Y₁-Y₁-Y₂-Y₂-Y₁-Y₃-Y₁-Y₃-Y₃-Y₁-Y₃-Y₁-Y₂-Y₃-Y₃

wherein

each Y₁ is independently selected from a hydroxy amino acid residue;

each Y₂ is independently selected from a sulfur containing amino acid residue; and

each Y₃ is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:

Z₁-Z₁-Z₂-Z₂-Z₁-Z₃-Z₁-Z₃-Z₃-Z₁-Z₃-Z₁-Z₃-Z₃

wherein

each Z₁ is independently selected from a hydroxy amino acid residue;

each Z₂ is independently selected from a sulfur containing amino acid residue; and

each Z₃ is independently selected from a basic amino acid residue, and fragments, analogs or derivatives of the peptide which bind HA.

28. (Amended) A method of preventing or reducing the metastasis of cancer cells comprising administering an effective amount of one or more hyaluronan-binding (HA binding) peptides [according to claim 1] to an animal in need thereof, wherein said HA binding peptide comprises:

(a) a sequence of the formula I:

X₁-X₂-X₁-X₃-X₄-X₃-X₄-X₃-X₃-X₅-X₆-X₆-X₁

wherein

each X₁ is independently selected from a hydroxy amino acid residue;

each X_2 is independently selected from a sulfur containing amino acid residue;

each X_3 is independently selected from a basic amino acid residue;

each X_4 is independently selected from an imino or aromatic amino acid residue;

each X_5 is independently selected from a dicarboxylic acid amino acid residue; and

each X_6 is independently selected from an aliphatic amino acid residue,

and fragments, analogs or derivatives of the peptide which can bind HA;

(b) a sequence of the formula II:

$Y_1 - Y_1 - Y_2 - Y_2 - Y_1 - Y_3 - Y_1 - Y_3 - Y_3 - Y_1 - Y_3 - Y_1 - Y_2 - Y_3 - Y_3$

wherein

each Y_1 is independently selected from a hydroxy amino acid residue;

each Y_2 is independently selected from a sulfur containing amino acid residue; and

each Y_3 is independently selected from a basic amino acid residue,

and fragments, analogs or derivatives of the peptide which bind HA; or

(c) a sequence of the formula III:

$Z_1 - Z_1 - Z_2 - Z_2 - Z_1 - Z_3 - Z_1 - Z_3 - Z_3 - Z_1 - Z_3 - Z_1 - Z_3 - Z_3$

wherein

each Z_1 is independently selected from a hydroxy amino acid residue;

each Z_2 is independently selected from a sulfur containing amino acid residue; and

each Z_3 is independently selected from a basic amino acid residue, and fragments,

analogs or derivatives of the peptide which bind HA.